Neonatal Survival 1

4 million neonatal deaths: When? Where? Why?

Joy E Lawn, Simon Cousens, Jelka Zupan, for the Lancet Neonatal Survival Steering Team*

The proportion of child deaths that occurs in the neonatal period (38% in 2000) is increasing, and the Millennium Development Goal for child survival cannot be met without substantial reductions in neonatal mortality. Every year an estimated 4 million babies die in the first 4 weeks of life (the neonatal period). A similar number are stillborn, and 0·5 million mothers die from pregnancy-related causes. Three-quarters of neonatal deaths happen in the first week—the highest risk of death is on the first day of life. Almost all (99%) neonatal deaths arise in low-income and middle-income countries, yet most epidemiological and other research focuses on the 1% of deaths in rich countries. The highest numbers of neonatal deaths are in south-central Asian countries and the highest rates are generally in sub-Saharan Africa. The countries in these regions (with some exceptions) have made little progress in reducing such deaths in the past 10–15 years. Globally, the main direct causes of neonatal death are estimated to be preterm birth (28%), severe infections (26%), and asphyxia (23%). Neonatal tetanus accounts for a smaller proportion of deaths (7%), but is easily preventable. Low birthweight is an important indirect cause of death. Maternal complications in labour carry a high risk of neonatal death, and poverty is strongly associated with an increased risk. Preventing deaths in newborn babies has not been a focus of child survival or safe motherhood programmes. While we neglect these challenges, 450 newborn children die every hour, mainly from preventable causes, which is unconscionable in the 21st century.

Of the 130 million babies born every year, about 4 million die in the first 4 weeks of life—the neonatal period.¹ A similar number of babies are stillborn—dving in utero during the last 3 months of pregnancy. Most neonatal deaths (99%) arise in low-income and middleincome countries, and about half occur at home. In poor communities, many babies who die are unnamed and unrecorded, indicating the perceived inevitability of their deaths. By contrast, the 1% of neonatal deaths that arise in rich countries are the subject of confidential inquiries and public outcry if services are judged substandard. Most trials of neonatal interventions focus on these few deaths in rich countries. The inverse care law, first described in the UK in the 1960s, remains valid: "The availability of good medical care tends to vary inversely with the need for it in the population served."2 For newborn babies, this law could appropriately be renamed the inverse information and care law: the communities with the most neonatal deaths have the least information on these deaths and the least access to cost-effective interventions to prevent them.

In this report, the first in a series of four on neonatal survival, we present epidemiological data to help guide efforts to reduce deaths of newborn children in countries where most of these deaths take place. This series follows the Bellagio child survival series,³ which emphasised the need for further work into neonatal deaths. It will also focus on strengthening of health systems (including community level) to provide care for newborn children in the highest mortality settings, and the costs of doing so. Our emphasis on neonatal survival is deliberate.⁴ We believe stillbirths, maternal morbidity and mortality, and neonatal morbidity are of great public-health importance. However, doing justice to all of these topics is not possible

in one series. We believe that increased attention to improving health systems around the time of childbirth will also reduce maternal deaths and stillbirths.

MDGs and newborn babies

The Millennium Development Goals (MDGs) represent the widest commitment in history to addressing global poverty and ill health.⁵ The fourth goal (MDG-4) commits the international community to reducing mortality in children aged younger than 5 years by two-thirds between 1990 and 2015. Between 1960 and 1990, the risk of dying in the first 5 years of life was halved—a major achievement in child health.⁶ However, achieving MDG-4 will depend on mortality reductions even greater in percentage terms than those achieved in the past (figure 1). A decade before the target date of 2015, many are already predicting the goal will not be met.⁷ Challenges include AIDS⁵ and increasing poverty, particularly in Africa, as well as a lack of global investment in child survival, despite 10.6 million deaths every year.⁹

Another challenge, less frequently identified in policy analysis, is the slow progress in reducing global neonatal mortality (figure 1). Child survival programmes in the developing world have tended to focus on pneumonia, diarrhoea, malaria, and vaccine-preventable conditions, which are important causes of death after the first month of life. Between 1980 and 2000, child mortality after the first month of life—ie, from month 2 to age 5 years—fell by a third, whereas the neonatal mortality rate (NMR) was reduced by only about a quarter. Hence, an increasing proportion of child deaths is now in the neonatal period; estimates for 2000¹ show that 38% of all deaths in children younger than age 5 years happen in the first month of life. Deaths in the first week of life have shown the least



Lancet 2005; 365: 891-900

See Comment

Published online March 3, 2005 http://image.thelancet.com/ extras/05art1073web.pdf

*Lancet Neonatal Survival Steering Team listed at end of article

Saving Newborn Lives/Save the Children-USA, and International Perinatal Care Unit, Institute of Child Health, London, Cape Town, South Africa (J E Lawn MRCP); London School of Hygiene and Tropical Medicine, London, UK (Prof S Cousens DipMathStat); and Department of Reproductive Health and Research, WHO, Geneva, Switzerland (J Zupan MD)

Correspondence to: Dr Joy E Lawn, Saving Newborn Lives/Save the Children-USA, and International Perinatal Care Unit, 11 South Way, Pinelands, Cape Town 7405, South Africa joylawn@yahoo.co.uk

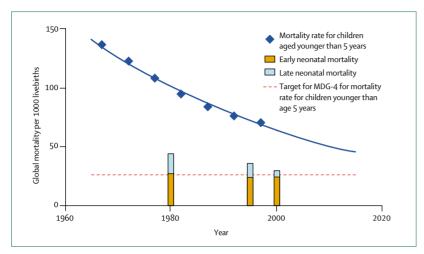


Figure 1: Meeting MDG-4: trends in child mortality among those younger than age 5 years¹ and in first 28 days of life,¹² 1965–2015

Trend for deaths in children younger than age 5 years fitted assuming constant proportional reduction every year.

progress. In 1980, only 23% of deaths arose in the first week of life; by the year 2000 this figure had risen to an estimated 28% (3 million deaths).

To meet MDG-4, a substantial reduction in NMRs in high-mortality countries is needed, and reducing deaths in the first week of life will be essential to progress. During the past decade, some regions of the world have made great progress in reducing NMRs (table 1).^{10,11} However, the inequity between rich and poor countries continues to increase, with lower NMRs and faster reductions in rich countries. There has been no measurable fall in the regional average NMR for sub-Saharan Africa. By contrast, the Americas achieved a 40% reduction in NMR largely because of progress in Latin America, where six countries have achieved reductions of 50% or more. In the western Pacific region, the largest percentage reductions have been recorded in Japan, South Korea, and Malaysia, all of which have low

	NMR per 1000 livebirths (range across countries)	Number (%) of neonatal deaths (1000s)	Percentage of deaths in children aged younger than 5 years in the neonatal period	Percentage change in NMR between 1996 and 2005 estimates*
Income groups				
High-income countries†	4 (1-11)	42 (1%)	63%	-29%
Low-income and	33 (2-70)	3956 (99%)	38%	-8%
middle-income countries				
WHO regions				
Africa	44 (9-70)	1128 (28%)	24%	5%
Americas	12 (4-34)	195 (5%)	48%	-40%
Eastern Mediterranean	40 (4-63)	603 (15%)	40%	-9%
Europe	11 (2-38)	116 (3%)	49%	-18%
Southeast Asia	38 (11-43)	1443 (36%)	50%	-21%
Western Pacific	19 (1-40)	512 (13%)	56%	-39%
Overall	30 (1-70)	3998 (100%)	38%	-16%

*The data inputs cover at least a 5 year period before each set of estimates. Period of change may be assumed to be up to 15 years. \dagger 39 countries with NMR data of 54 countries with gross national income per person of >US\$9386. 10

Table 1: Regional or country variations in NMRs and numbers of neonatal deaths, showing the proportion of deaths in children younger than age 5 years 19-11

NMRs (<5 per 1000 livebirths). The picture in Asia is mixed. In southeast Asia, many countries have reduced neonatal mortality; in some cases, such as Indonesia, reduction has been considerable (about 50%). In the countries of south-central Asia, with the exceptions of Bangladesh and Sri Lanka (which achieved about 40% reductions), more limited advances have been recorded.1,10 India, for example, where more than a quarter of the world's neonatal deaths take place, has seen a reduction of just 11%. India's modest drop in NMR is largely the result of late neonatal mortality reductions (deaths after the first week of life), in part due to a fall in deaths from tetanus. Globally, neonatal tetanus deaths have fallen by 50% since 1990. By 2000, two-thirds of low-income and middle-income countries had eliminated neonatal tetanus, and an additional 22 countries were nearing this goal; two-thirds of the remaining high-incidence countries are in Africa.12

A similar pattern over time of fairly rapid reductions in post-neonatal mortality, steady reductions in late neonatal mortality, and slower reductions in early neonatal mortality was seen in industrialised countries in the mid-20th century. Neonatal tetanus was eliminated in highincome countries before vaccination was available. In England the NMR fell from more than 30 per 1000 livebirths in 1940, to ten per 1000 in 1975, coinciding with the introduction of free antenatal care, improved childbirth care, and the availability of antibiotics.13 Neonatal intensive care became available only after the NMR had fallen below 15. Substantial global reductions in neonatal deaths in the next decade will depend on increasing coverage with interventions that improve neonatal survival within the context of maternal and child health programmes. Information is needed to identify priorities: where, when, and why do newborn babies die?

Where do newborn babies die?

Most neonatal deaths are unrecorded in any formal registration system, hence global analysis is based on estimates (panel 1).¹⁴⁻¹⁷ The most recent estimates suggest that there were nearly 4 million neonatal deaths in 2000. Only 1% of these deaths were in 39 high-income countries, where the average NMR is four per 1000 livebirths (table 1). The remaining 99% of deaths were in low-income and middle-income countries, where the average NMR is estimated to be 33.¹

About two-thirds of neonatal deaths arise in the African and southeast Asian regions of WHO (table 1). The countries with the largest absolute numbers of deaths are mainly in south Asia, because of the large populations in this region; India alone contributes a quarter of neonatal deaths. Ten countries account for two-thirds of neonatal deaths (table 2). However, the countries with the highest rates of neonatal mortality are mostly in sub-Saharan Africa (14 of the 18 countries with NMRs >45 per 1000; figure 2). Especially high NMRs are seen in countries with recent civil unrest,

Panel 1: Data inputs and methods used to obtain estimates for this report

Counting neonatal deaths

Background

Few neonatal deaths arise in countries with high coverage (>90%) vital registration. Information for most neonatal deaths comes from household surveys, particularly DHS, which use cluster sampling to produce nationally representative estimates. For some countries, often those with current or recent instability, there are no reliable population-based data, and estimation by statistical modelling is the only option.

Inputs

New estimates of the number of neonatal deaths by country produced by WHO; less than 5% of estimates come from countries with high coverage vital registration, 75% are based on DHS data, and 20% are derived from estimates of deaths of children younger than age 5 years adjusted for HIV prevalence. More detailed explanation is given elsewhere.

Limitations

Neonatal deaths are less likely to be recorded if a baby dies in the first hours or days after birth¹⁴ or is very small.¹⁵ Misclassification between stillbirths and neonatal deaths is also possible. In some settings, this misclassification might be deliberate to avoid filling a death certificate that would be required if a neonatal death is declared. Assessments of the validity of retrospective surveys suggest that in poor settings in south Asia they might greatly underestimate neonatal deaths.¹⁶ Reporting of time of death is prone to inconsistencies in recording in the first 24 h, which might be coded as day 0 or day 1, and by heaping on certain days (7, 14, 21, and 30).

Causes of neonatal deaths

Background

Less than 3% of neonatal deaths arise in countries with high-coverage vital registration and reliable, recent data on causes of neonatal deaths. For the remaining 97%, estimation is the only option and the limited quantity and quality of the input data results in inherent uncertainty.

Inputs

We examined two sources of data on causes of neonatal deaths—vital registration datasets for countries with high coverage (>90%) and studies identified through systematic searches of published work and unpublished datasets. Data from 45 vital registration systems (96 797 neonatal deaths) and 56 studies (29 countries, 13 685 neonatal deaths) were included and mapped onto seven cause categories—severe infection, tetanus, diarrhoea, asphyxia, preterm birth, congenital, and other. We used multinomial regression to model the proportion of deaths due to every cause for every data source. We used the vital registration-based model to estimate the distribution of causes of death for 22 low-mortality countries without national data, and used a study-based model to obtain estimates for 115 high-mortality countries. Uncertainty estimates were derived with the jack-knife approach. Details are given elsewhere. The countries without national data and used a study-based model to obtain estimates for 115 high-mortality countries.

Limitations

Allocation of one death to one cause is somewhat artificial when multiple causes act synergistically, and the rules applied by different coders for allocation of coexisting causes are not always clear. To be programmatically useful, recorded causes of death should relate to prevention or management—if a moderately preterm infant dies of infection, then infection is the key cause to address. However, in a very preterm infant, infection management alone is unlikely to avert their death.

Other data inputs

We based analysis of DHS data for time of death, attendance at birth, socioeconomic status, and sex on 47 downloadable datasets published since 1995 (http://www.measuredhs.com), and restricted it to births in the 5 years before the survey. All analyses were done in Stata version 8. Analysis of maternal risk factors for neonatal and perinatal mortality was based on a systematic search of the published work and was restricted to population-based studies in settings without neonatal intensive care and which reported effect estimates adjusted for major potential confounders.

such as Sierra Leone and Liberia. The proportion of deaths in children younger than age 5 years that takes place in the neonatal period varies between regions, being much higher in southeast Asia (47%) than in sub-Saharan Africa (26%), although these regions have similar NMRs (table 1).

When do newborn babies die?

The neonatal period is only 28 days and yet accounts for 38% of all deaths in children younger than age 5 years.

The remaining 62% of deaths in this age group arise over a period of almost 1800 days. Thus, the average daily mortality rate during the neonatal period is close to 30-fold higher than during the post-neonatal period. Even within the neonatal period there is considerable variation in the daily risk of death (figure 3). Mortality is very high in the first 24 h after birth (25–45% of all neonatal deaths in this analysis). Globally some three-quarters of neonatal deaths happen in the first week after birth.¹

	Number of neonatal deaths (1000s)	Percentage of global neonatal deaths (n=3·99 million)	NMR (per 1000 livebirths)
India	1098	27%	43
China	416	10%	21
Pakistan	298	7%	57
Nigeria	247	6%	53
Bangladesh	153	4%	36
Ethiopia	147	4%	51
Democratic Republic of the Congo	116	3%	47
Indonesia	82	2%	18
Afghanistan	63	2%	60
United Republic of Tanzania	62	2%	43
Total	2682	67%	

Why do newborn babies die?

Direct causes of death

Less than 3% of neonatal deaths take place in countries with vital registration data reliable for cause-of-death analysis. Population-based information in highmortality settings is largely dependent on verbal autopsy methods of variable quality. Global estimates are only possible through statistical modelling. Estimates from 2000 of the distribution of direct causes of death (figure 4) indicate that preterm birth (28%), severe infections (36%, including sepsis/pneumonia [26%], tetanus [7%], and diarrhoea [3%]), and complications of asphyxia (23%) account for most neonatal deaths. Of the remaining 14%, 7% of deaths were related to congenital abnormalities. 16

The distribution of causes of neonatal death varies between countries, correlating with the degree of neonatal mortality (figure 5). In very high-mortality settings (NMR >45), almost 50% of deaths are due to severe infection, tetanus, and diarrhoea. At low NMR levels (NMR <15), sepsis/pneumonia accounts for less than 20% of deaths, and tetanus and diarrhoea are almost non-existent as causes of neonatal death. The risk of neonatal death due to severe infection in very highmortality countries is about 11-fold the risk in lowmortality countries. The risk of dying due to birth asphyxia is about eight times higher for babies in countries with very high NMRs, even though the proportion of such neonatal deaths is fairly constant across mortality levels. The proportion of deaths due to prematurity drops with increasing NMR, but this fall is due to the large number of deaths from infection in high-NMR countries. In a country with a very high NMR, the risk of death due to prematurity is still three times higher than in low-mortality countries. In addition to variation between countries in the distribution of causes, there is often substantial variation within countries. In the countries with continuing high rates of neonatal tetanus, for example, most of these deaths arise in only a few districts, and in poorer populations with limited health care.12

Low birthweight

Only about half of babies are weighed at birth, and a smaller proportion is of known gestational age.¹⁸

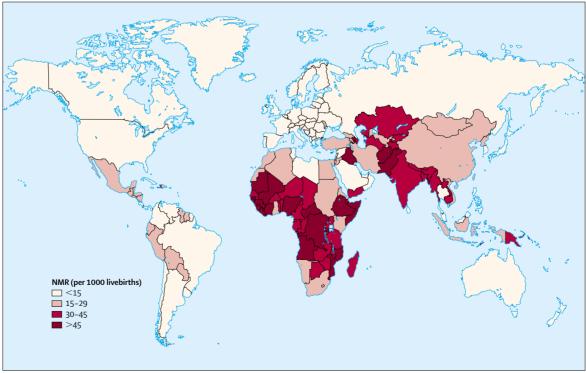


Figure 2: Variation between countries in NMRs

18 million babies are estimated to be born with low birthweights every year-half in south Asia.9 Although these low-birthweight babies constitute only about 14% of children born, they account for 60-80% of neonatal deaths.¹⁶ Low birthweight arises through short gestation (preterm birth) or in-utero growth restriction, or both.¹⁹ We estimate that 28% of neonatal deaths globally are directly attributable to preterm birth (figure 4). Results of an analysis of vital registration data (45 countries, 96 797 deaths) and of five population-based datasets, including two from south Asia (883 neonatal deaths). 20-22 suggest that at most 1-2% of neonatal deaths are directly attributable to in-utero growth restriction in term neonates (CHERG neonatal group, unpublished data). Prematurity and in-utero growth restriction are also indirect causes or risk factors for neonatal deaths, especially those due to infection. Taking into account deaths both directly and indirectly attributable to prematurity and in-utero growth restriction, a study in Bangladesh reports that the risk of death was several-fold higher in preterm infants than in full-term infants whose growth had been restricted in utero (risk ratio 4.78, 95% CI 3.14-7.27).23 Attempts to reduce the proportion of babies born with low birthweights at the population level, in general, have been met with little success.24 However, most deaths in moderately preterm babies and in those born at term but whose growth had been restricted in utero can be prevented with extra attention to warmth, feeding, and prevention or early treatment of infections.^{25–27} Complex technology is not a prerequisite.

Maternal health and intrapartum complications

Maternal health and health care are important determinants of neonatal survival. Neonatal outcomes are affected by health throughout the lifecycle, starting with the girl child, through adolescence and pregnancy.^{28,29} Complications during labour are an important determinant of fetal and neonatal survival and health.30 In general, intrapartum risk factors are associated with greater increases in risk of neonatal death than those identified during pregnancy, which are in turn associated with greater increases in risk than prepregnancy factors (table 3).30-42 Obstructed labour and malpresentation carry the highest risk and require skilled intervention. The death of a mother substantially increases the risk of death for her newborn child. In one study,42 reporting child outcomes for mothers who died in labour, all the newborn babies (n=9) died within 1 year of birth.

Neonatal mortality and gender

Girls have a well described biological survival advantage in the neonatal period.⁴³ Reduced care seeking for girls compared with boys has been reported, especially in south Asia.^{44,45} Analysis of DHS data (not shown) does not provide evidence of a reduction in girls' survival

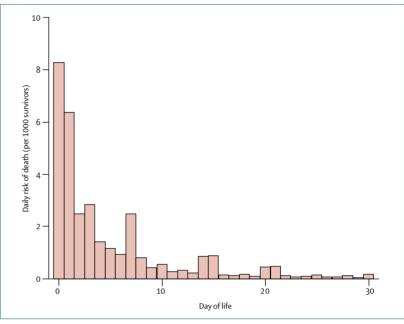


Figure 3: Daily risk of death during first month of life based on analysis of 47 DHS datasets (1995–2003) with 10 048 neonatal deaths

Deaths in first 24 h recorded as occurring on day 0, or possibly day 1, depending on interpretation of question and coding of response. Preference for reporting certain days (7, 14, 21, and 30) is apparent.

advantage at the national level. Female infanticide has been reported from rural China 46,47 and south Asia, 48 but the true incidence of this practice is unknown. Sex discrimination before birth through sex-selective abortion is well documented; this practice has been reported in India 48 and China, 49 where 17% more boys are born than girls, resulting in an estimated excess of 1.7 million male babies per year.

Poverty and neonatal mortality

Poverty is an underlying cause of many neonatal deaths, either through increasing the prevalence of risk factors such as maternal infection, or through reducing access to effective care. However, poverty is not just a problem

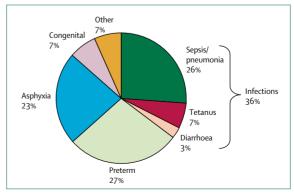


Figure 4: Estimated distribution of direct causes of 4 million neonatal deaths for the year 2000

Based on vital registration data for 45 countries and modelled estimates for 147 countries.

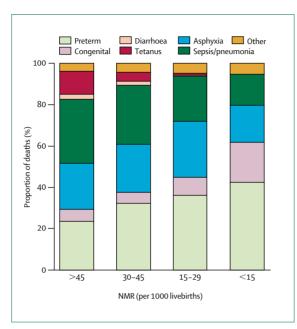


Figure 5: Estimated distribution of causes of neonatal death for 192 countries, according to degree of neonatal mortality¹⁷

	Adjusted odds ratio*
Life-cycle factors	
Maternal age (years)	1.1-2.3
<18	1-3-2-0
>35	
Maternal size	
Height <150 cm	1-3-4-8
Prepregnancy weight <47 kg	1-1-2-4
Parity	
Primigravida	1-3-2-2
Parity >6	1.4-1.5
Poor obstetric history (previous perinatal death or instrumental delivery)	1.6-3.5
Antenatal factors	
Multiple pregnancy	2-0-6-8
Hypertensive disorders	
Pre-eclampsia	1.7-3.7
Eclampsia	2.9-13.7
Bleeding per vagina after 8th month	3-4-5-7
Maternal jaundice	2.0-7.9
Maternal anaemia (PCV <0.21)	1.9-4.2
Maternal anaemia (PCV <33%)	NS in 4 studies
Maternal malaria (blood test positive)	2-2-3-5†
Syphilis (perinatal death)	1.7-5.8
HIV (infant death)	7-2
Intrapartum factors	
Malpresentation	
Breech	6-4-14-7
Other	8-3-33-5
Obstructed labour/dystocia	6-7-84-9
Prolonged second stage	2.6-4.8
Maternal fever during labour (>38°C)	9-7-10-2
Rupture of membranes >24 h	1.8-6.7
Meconium staining of liquor	11.5

PCV=packed cell volume; NS=not significant. *Odds ratios included are from population-based studies adjusting for major confounders (parity and socioeconomic status) and significantly associated with intrapartum stillbirth or neonatal death or perinatal death unless given as NS in more than one study. †Risk for low birthweight not mortality.

 $\it Table~3: Adjusted~odds~ratios~for~various~risk~factors~for~neonatal~or~perinatal~death~reported~from~population-based~studies^{31-43}$

in poor countries. Results of a Canadian study⁵⁰ suggest a disparity in stillbirths and neonatal deaths between the richest and poorest 20% of the population that has persisted for almost 20 years. DHS data from 20 countries in sub-Saharan Africa and three large countries in south Asia reveal consistently higher NMRs for those in the poorest 20% of households than for those in the top quintile. In general, the disparity is higher for postneonatal than for neonatal deaths. If the NMRs noted for the richest 20% of the population in every country were seen in the entire population of that country then NMRs would be reduced by 19% (median across 20 countries, IQR 9-28) in Africa and 28%, 41%, and 43% in Bangladesh, India, and Nepal, respectively. These reductions would prevent an estimated 0.5 million neonatal deaths in these three Asian countries alone and an additional 219 000 in Africa. Addressing inequity should be a priority of all strategies for improving survival of newborn babies.

Neonatal mortality and health-care coverage

The relative importance of different causes of death varies with NMR (figure 5). So too does the coverage of skilled attendance and the proportion of births that take place in a health facility (table 4). Globally, 56% of women deliver with a skilled attendant, but the variation between countries is very great (5-99%).51 Skilled attendance and institutional delivery rates are lowest in countries with the highest NMRs. In sub-Saharan Africa, less than 40% of women deliver with skilled care and in south Asia the figure is less than 30%. Across 40 countries with DHS data between 1995 and 2003. more than 50% of neonatal deaths arose after a home birth with no skilled care. Within sub-Saharan African and south Asian countries for which DHS data are available, the NMR is consistently higher and the coverage of skilled care consistently lower in rural areas.

The three-delays model—delay in recognition of illness, delay in seeking and accessing care, and delay in the provision of care once at a health facility—has helped in understanding maternal deaths.⁵² Similar delays have been documented for young infants with severe illness and, with the rapid progression of many neonatal illnesses, certainly play an important part in neonatal deaths. Among 182 child deaths in rural Guinea, more than 90% of post-neonatal children with pneumonia were taken for outside care, whereas only 60% of newborn babies (16 of 26) with severe infection were taken out of the home for care.⁵³ In a Ugandan study,⁵⁴ only 21% (15 of 71) of severely ill babies completed referral as advised.⁵⁵ The most common reason for not completing referral (90%) was lack of money.

Using information in policy and programmes

Epidemiology provides a basis for understanding and reducing ill health. Some of the programmatic implications of the data presented here are outlined in

	Mortality setting				
	NMR >45	NMR 30-45	NMR 15-29	NMR <15	
Numbers of neonatal deaths (1000s) (number of countries)	1147 (18)	1759 (39)	838 (40)	254 (95)	
nstitutional delivery, median coverage (IQR)*	33% (16-49)	48% (18-78)	65% (51-91)	98% (95-99)	
5killed attendance at birth, median coverage (IQR)*	41% (22-44)	50% (27-77)	85% (62-96)	99% (95-100)	
Fraditional birth attendants present, median coverage (IQR)†	20% (18-25; 7 countries)	18% (8-37; 21 countries)	9% (1-31; 16 countries)	9% (9-41; 3 countries)	

panel 2. The reduction of neonatal mortality over the past 20 years has been inadequate, especially for deaths during the first week of life and particularly in the poorest countries. Every year, 4 million babies still die in their first 4 weeks of life, most from preventable causes. This number is double the deaths due to HIV/AIDS; although AIDS is rightly hailed as a global emergency, newborn deaths are largely ignored.

Since neonatal deaths account for 24–56% of deaths in children younger than age 5 years across the six WHO regions, no region can afford to ignore them. Further reductions in child mortality will depend on substantial improvements in neonatal survival; current approaches have had some success in preventing late neonatal deaths, but have had little effect on early neonatal deaths in high-mortality settings. Although post-neonatal deaths and late neonatal deaths are amenable to public health interventions—eg, immunisation, breastfeeding, and improved hygiene—the achievement of major reductions in early neonatal (and maternal) deaths will depend on provision of individualised clinical care, which is much more challenging but could reduce NMRs to 15 per 1000 or less without complex technology.¹³

Early neonatal deaths account for 75% of all neonatal deaths, and preventing these depends on attention to the causes of death that are unique to the first week of life, particularly birth asphyxia and prematurity. Many neonatal deaths take place within the first 24 h after birth—at least 1 million per year. A large proportion of 4 million stillbirths occur as intrapartum stillbirths and an estimated 515 000 maternal deaths occur, over 75% of which are intrapartum or in the postnatal period. 55,56 Yet in sub-Saharan Africa and southeast Asia, where two-thirds of neonatal deaths happen, between a quarter and a third of women deliver with a skilled attendant, and even fewer have access to emergency obstetric and neonatal care. The poorest people within these countries are even worse off than these average figures imply: in the highest mortality countries, a median of 14% of women have skilled care at birth; among the richest 20% of women in these countries, a median of 86% have skilled care. To achieve major reductions in early neonatal mortality in such settings, coverage of care during childbirth and the early postnatal period should be increased to reach the poorest, and most underserved populations. Such action would probably also reduce maternal deaths (contributing to

Panel 2: Key messages for neonatal health

How many deaths?

4 million neonatal deaths occur every year. Reducing these deaths is a moral imperative and essential for achievement of MDG-4.

When?

38% of deaths in children aged younger than 5 years arise in the first month of life.

Between a quarter and half of all neonatal deaths happen within 24 h of birth.

Three-quarters of neonatal deaths arise in the first week of life.

Where

99% of individuals die in low-income and middle-income countries, with limited information for decision-making.

Two-thirds of deaths occur in only ten countries.

At least half of neonatal deaths arise after home births.

Why?

The major direct causes of neonatal deaths globally are infections (36%), preterm birth (28%), and asphyxia (23%). The distribution of causes of neonatal death varies with the degree of neonatal mortality.

60–80% of neonatal deaths arise in low birthweight babies. Reduction of mortality among moderately preterm and term in-utero growth restriction infants is feasible without complex technology.

Maternal complications, especially during childbirth, carry a high risk of neonatal death.

Elimination of the mortality gap between the richest and poorest within countries in sub-Saharan Africa and within three south Asian countries could avert almost 0.75 million deaths.

MDG-5) and stillbirths. The constraints to scaling up neonatal and maternal health care in countries and reaching the poorest will be analysed by Knippenberg and colleagues as part of this series.⁵⁷

Late neonatal deaths are mainly due to infections. Case management of neonatal infections is mainly provided through child-health services, both in facilities and through family-community care. Remarkable progress has been made in reducing neonatal tetanus, but elimination is an unfinished global commitment, originally scheduled for 1995, then broadened to maternal and neonatal tetanus and postponed to 2005. Neonatal tetanus is now responsible for a small proportion of global neonatal deaths (6%) and is almost exclusively a disease of the poor. It is eminently preventable, but the world looks set to miss the elimination target for a second time, while rolling out much more expensive interventions, such as prevention of mother-to-child transmission of HIV/AIDS.

Improving information for decision making

Increasing the availability and use of relevant information in programmes and policy is essential if health care for newborn babies and their mothers is to be improved. These WHO NMR estimates are the first official estimates of neonatal deaths since 1995.11 Mortality estimates for children aged vounger than 5 years are released yearly. and estimates of other major groups—such as maternal deaths and deaths related to HIV/AIDS—are published every 2–5 years. 58-60 The estimation process is timeconsuming, but an absence of consistent periodic estimates leads to invisibility, and invisibility contributes to inaction. The child survival publicity of several major health policy organisations and even the official website of the MDGs does not mention the major causes of neonatal deaths (http://www.developmentgoals.org). In the widely used WHO pie chart, detailing causes of death for children younger than age 5 years, the largest category—other—is mainly the invisible neonatal causes (http://www.who.int/child-adolescent-health). The second largest category—perinatal causes—is poorly understood: few realise this category includes asphyxia and preterm birth, but excludes stillbirths.

Better data than presently available are also needed at service delivery and national level to manage programmes and achieve maximum effectiveness of often scarce resources. Programme managers cannot manage what they cannot count.⁶¹ The term neonatal describes a time period—not a cause—and prevention of neonatal deaths will depend on various strategies to address specific causes. Information on causes of neonatal death is important for reducing deaths of newborn babies. Cause-specific mortality varies between settings, yet in many places such information is not available and can be expensive and difficult to obtain through surveys and verbal autopsy questionnaires.⁶² Simplified and consistent verbal autopsy methods are needed, but are mainly applicable in research settings.

In the absence of such data, the NMR might be useful as a simple predictor of the distribution of causes of neonatal mortality (figure 4). Since NMRs are also strongly (inversely) correlated with skilled attendance at birth, they might be useful in guiding programme design. These associations will be explored further in the third article of this series.⁵⁷

Relevant information does exist at many levels of care, but is often not used. For example, the register of births kept in almost every health facility at which deliveries take place could be used to provide information about intrapartum stillbirths and early neonatal deaths.61 Identifying and addressing avoidable causes of death is possible even in poorly functioning health systems. 63 At the state or national level, many countries have DHS NMR estimates, but national decision makers might not be aware of, or able to access, them.⁶⁴ Stillbirths should also be counted, in their own right and because misclassification can arise between stillbirths and neonatal deaths.65 Additionally, if intrapartum interventions prevent some stillbirths early neonatal deaths might initially increase. Unless both outcomes are tracked, erroneous programme decision making could result.

Conclusion

Real progress in reducing deaths of newborn babies will depend on higher coverage of services in the highest-mortality countries, for the poorest people, and at the time of greatest risk—birth and the first days of life. What works, though, and what should the priorities be? Analysis of the evidence, cost, and feasibility of interventions is needed and is the focus of the next paper in this series. For Improved epidemiological data are essential, but social visibility is also important—once communities and decision makers perceive high neonatal (and maternal) deaths as an issue, public ownership of the problem and progress will be more likely. The While we do not address these challenges, 450 newborn babies die every hour, most from preventable causes, which is unconscionable in the 21st century.

Lancet Neonatal Survival Steering Team

Joy E Lawn, Simon Cousens, Zulfiqar A Bhutta, Gary L Darmstadt, Jose Martines, Vinod Paul, Rudolph Knippenberg, and Helga Fogstad

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

We thank Prof R Black (Johns Hopkins School of Public Health, MA, USA) and Prof B R Kirkwood (London School of Hygiene and Tropical Medicine, London, UK) for insightful reviews of this report at the newborn series review meeting; Katarina Wilczynska-Ketende for CHERG neonatal work; Trevor Croft (UNICEF, NY, USA) for advice about DHS analysis and Kenji Shibuya, Elizabeth Ahman, Mie Inoue, and Doris Mafat (WHO, Geneva, Switzerland) for supplying additional data and information; and David Osrin (Institute of Child Health, London, UK) for helpful comments on an early draft.

JEL was supported by the Bill & Melinda Gates Foundation through a grant to Save the Children Federation for the Saving Newborn Lives Initiative. The cause of death analysis was done by JEL and SC with the

CHERG neonatal group, funded by the Gates Foundation and WHO, Child and Adolescent Health. Additional work for this report was supported directly by the Gates Foundation and by USAID though a grant to Johns Hopkins University through the Global Research Activity. The funding sources did not influence the content of this article.

References

- Zupan J, Aahman E. Perinatal mortality for the year 2000: estimates developed by WHO. Geneva: World Health Organization, 2005.
- 2 Hart JT. The inverse care law. Lancet 1971; 1: 405-12.
- 3 Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? *Lancet* 2003; 361: 2226–34.
- 4 Lawn JE, Cousens S, Bhutta ZA, et al. Why are 4 million newborn babies dying each year? *Lancet* 2004; 364: 399–401.
- 5 Haines A, Cassels A. Can the millennium development goals be attained? BMJ 2004; 329: 394–97.
- 6 Ahmad OB, Lopez AD, Inoue M. The decline in child mortality: a reappraisal. Bull World Health Organ 2000; 78: 1175–91.
- 7 Travis P, Bennett S, Haines A, et al. Overcoming health-systems constraints to achieve the Millennium Development Goals. *Lancet* 2004: 364: 900–06.
- Claeson M, Gillespie D, Mshinda H, Troedsson H, Victoria CG. Knowledge into action for child survival. *Lancet* 2003; 362: 323–27.
- 9 UNICEF. State of the World's Children 2005. New York: UNICEF, 2004.
- 10 The World Bank Group. Data and statistics: country groups. http://www.worldbank.org/data/countryclass/classgroups.htm#High_income (accessed Jan 12, 2005).
- 11 WHO. Perinatal mortality: a listing of available information. Geneva: World Health Organization, 1996.
- 12 UNICEF. Maternal and neonatal tetanus elimination by 2005: strategies for achieving and maintaining elimination. New York: UNICEF. 2000.
- 13 MacFarlane A, Johnsone A, Mugford M. Epidemiology. In: Rennie JM, Roberton NRC, eds. Textbook of Neonatology. Cambridge: Churchill Livingstone, 1999: 3–33.
- 14 Lumbiganon P, Panamonta M, Laopaiboon M, Pothinam S, Patithat N. Why are Thai official perinatal and infant mortality rates so low? *Int J Epidemiol* 1990; 19: 997–1000.
- 15 McCarthy B, Terry J, Rochat RW, Quave S, Tyler C. The underregistration of neonatal deaths: Georgia 1974–77. Am J Public Health 1980; 70: 977–82.
- 16 Bang A, Reddy MH, Deshmukh MD. Child mortality in Mahararshtra. Economic Political Weekly 2002; 37: 4947–65.
- 17 Lawn JE, Cousens SN, Wilczynska K. Estimating the causes of four million neonatal deaths in the year 2000: statistical annex—the world health report 2005. Geneva: World Health Organization, 2005.
- 18 Blanc AK, Wardlaw T. Monitoring low birth weight: an evaluation of international estimates and an updated estimation procedure. Bull World Health Organ (in press).
- 19 Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis Bull World Health Organ 1987; 65: 663–737.
- 20 Datta N, Mand M, Kumar V. Validation of causes of infant death in the community by verbal autopsy. *Indian J Pediatr* 1988; 55: 599–604
- 21 el Shafei AM, Sandhu AK, Dhaliwal JK. Perinatal mortality in Bahrain. Aust N Z J Obstet Gynaecol 1988; 28: 293–98.
- 22 el Zibdeh MY, Al Suleiman SA, Al Sibai MH. Perinatal mortality at King Fahd Hospital of the University Al-Khobar, Saudi Arabia. Int J Gynaecol Obstet 1988; 26: 399–407.
- 23 Yasmin S, Osrin D, Paul E, Costello A. Neonatal mortality of low-birth-weight infants in Bangladesh. Bull World Health Organ 2001; 79: 608–14.
- 24 Kramer MS. The epidemiology of adverse pregnancy outcomes: an overview. J Nutr 2003; 133(5 suppl 2): 1592S–6S.
- 25 Aleman J, Brannstrom I, Liljestrand J, Pena R, Persson LA, Steidinger J. Saving more neonates in hospital: an intervention towards a sustainable reduction in neonatal mortality in a Nicaraguan hospital. *Trop Doct* 1998; 28: 88–92.

- 26 Duke T, Willie L, Mgone JM. The effect of introduction of minimal standards of neonatal care on in-hospital mortality. P N G Med J 2000: 43: 127–36.
- 27 Conde-Agudelo A, Diaz-Rossello JL, Belizan JM. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2003. Oxford: Update Software.
- 28 Bacci A, Manhica GM, Machungo F, Bugalho A, Cuttini M. Outcome of teenage pregnancy in Maputo, Mozambique. Int J Gynaecol Obstet 1993; 40: 19–23.
- 29 United Nations Administrative Committee on Coordination/Subcommittee on Nutrition. Low birth weight: report of a meeting. Geneva: ACC/SCN in collaboration with ICCDR,B: 2000. http://www.healthynewborns.org/section/tools/ research/interventions/lbw (accessed Feb 4, 2005).
- 30 Kusiako T, Ronsmans C, Van der PL. Perinatal mortality attributable to complications of childbirth in Matlab, Bangladesh. Bull World Health Organ 2000; 78: 621–27.
- 31 Barros FC, Victora CG, Vaughan JP, Estanislau HJ. Perinatal mortality in southern Brazil: a population-based study of 7392 births. Bull World Health Organ 1987; 65: 95–104.
- 32 Chalumeau M, Salanave B, Bouvier-Colle MH, De Bernis L, Prual A, Breart G. Risk factors for perinatal mortality in West Africa: a population-based study of 20326 pregnancies. Acta Paediatr 2000; 89: 1115–21.
- 33 Kulmala T, Vaahtera M, Rannikko J, et al. The relationship between antenatal risk characteristics, place of delivery and adverse delivery outcome in rural Malawi. Acta Obstet Gynecol Scand 2000; 79: 984–90.
- 34 Vanneste AM, Ronsmans C, Jyotsnamoy C, Francisco A. Prenatal screening in Bangladesh: moving from prediction to care. Health Pol Plann 2000; 15: 1–10.
- 35 McDermott J, Steketee R, Wirima J. Perinatal mortality in rural Malawi. Bull World Health Organ 1996; 74: 165–71.
- 36 Bloland P, Slutsker L, Steketee RW, Wirima JJ, Heymann DL, Breman JG. Rates and risk factors for mortality during the first two years of life in rural Malawi. Am J Trop Med Hyg 1996; 55 (suppl 1): 82–86.
- 37 Steketee RW, Nahlen BL, Parise ME, Menendez C. The burden of malaria in pregnancy in malaria-endemic areas. Am J Trop Med Hyg 2001; 64 (suppl 1–2): 28–35.
- 38 Verhoeft FH, Brabin BJ, Chimsuku L, et al. Malaria in pregnancy and its consequences for the infant in rural Malawi. Ann Trop Med Parasitol 1999; 93 (suppl 1): S25–33.
- 39 Bam RH, Cronje HS, Muir A, Griessel DJ, Hoek BB. Syphilis in pregnant patients and their offspring. Int J Gynaecol Obstet 1994; 44: 113–18.
- 40 Lumbiganon P, Piaggio G, Villar J, et al. The epidemiology of syphilis in pregnancy. *Int J STD AIDS* 2002; **13**: 486–94.
- 41 Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet* 2004; 364: 1336-43
- 42 Greenwood AM, Greenwood BM, Bradley AK, et al. A prospective survey of the outcome of pregnancy in a rural area of the Gambia. Bull World Health Organ 1987; 65: 635–43.
- 43 Ulizzi L, Zonta LA. Sex differential patterns in perinatal deaths in Italy. *Hum Biol* 2002; 74: 879–88.
- 44 Nielsen BB, Liljestrand J, Hedegaard M, Thilsted SH, Joseph A. Reproductive pattern, perinatal mortality, and sex preference in rural Tamil Nadu, south India: community based, cross sectional study. BMJ 1997; 314: 1521–24.
- 45 Victora CG, Wagstaff A, Schellenberg JA, Gwatkin D, Claeson M, Habicht JP. Applying an equity lens to child health and mortality: more of the same is not enough. *Lancet* 2003; 362: 233–41.
- 46 Xu B, Rantakallio P, Jarvelin MR, Fang XL. Sex differentials in perinatal mortality in China and Finland. Soc Biol 1997; 44: 170–78.
- 47 Wu Z, Viisainen K, Wang Y, Hemminki E. Perinatal mortality in rural China: retrospective cohort study. *BMJ* 2003; **327**: 1319.
- 48 Sarkar ML. Female foeticide. J Indian Med Assoc 2002; 100: 52.
- 49 Plafker T. Sex selection in China sees 117 boys born for every 100 girls. BMJ 2002; 324: 1233.

- 50 Luo ZC, Kierans WJ, Wilkins R, Liston RM, Mohamed J, Kramer MS. Disparities in birth outcomes by neighborhood income: temporal trends in rural and urban areas, British Columbia. *Epidemiology* 2004; 15: 679–86.
- 51 UNICEF. State of the world's children report 2001. New York: UNICEF. 2000.
- 52 Thaddeus S, Maine D. Too far to walk: maternal mortality in context. Soc Sci Med 1994; 38: 1091–110.
- 53 Schumacher R, Swedberg E, Diallo MO, Keita DR, Kalter H, Pasha O. Mortality Study in Guinea: investigating the causes of death for children under 5. Washington: Save the Children Federation, 2002.
- 54 Peterson S, Nsungwa-Sabiiti J, Were W, et al. Coping with paediatric referral: Ugandan parents' experience. *Lancet* 2004; 363: 1955–56.
- 55 Li XF, Fortney JA, Kotelchuck M, Glover LH. The postpartum period: the key to maternal mortality. *Int J Gynaecol Obstet* 1996; 54: 1–10.
- 56 AbouZhar C, Wardlaw T. Maternal mortality in 2000: estimates developed by WHO, UNICEF and UNFPA. Geneva: World Health Organization, 2003.
- 57 Knippenberg R, Lawn JE, Darmstadt GL, et al. Systematic scaling up of neonatal care in countries. Published online March 3, 2005. http://image.thelancet.com/extras/05art1164web.pdf.
- 58 UNICEF. The state of the world's children, 2004: girls, education and development. New York: UNICEF, 2004.
- 59 Walker N, Grassly NC, Garnett GP, Stanecki KA, Ghys PD. Estimating the global burden of HIV/AIDS: what do we really know about the HIV pandemic? *Lancet* 2004; 363: 2180–85.

- 60 Hill K, AbouZhar C, Wardlaw T. Estimates of maternal mortality for 1995. Bull World Health Organ 2001; 79: 182–93.
- 61 Lawn JE, McCarthy B, Ross SR. The healthy newborn: a reference guide for program managers. Atlanta: CDC and CARE, 2001.
- 62 Sibai AM. Mortality certification and cause-of-death reporting in developing countries. Bull World Health Organ 2004; 82: 83.
- 63 Bugalho A, Bergstrom S. Value of perinatal audit in obstetric care in the developing world: a ten-year experience of the Maputo model. Gynecol Obstet Invest 1993; 36: 239–43.
- 64 Godlee F, Pakenham-Walsh N, Ncayiyana D, Cohen B, Packer A. Can we achieve health information for all by 2015? *Lancet* 2004; 364: 295–300.
- 65 Kramer MS, Liu S, Luo Z, Yuan H, Platt RW, Joseph KS. Analysis of perinatal mortality and its components: time for a change? Am J Epidemiol 2002; 156: 493–97.
- 66 Darmstadt GL, Bhutta ZA, Cousens S, Adam T, Walker N, de Bernis L for the Lancet Neonatal Survival Steering Team. Evidence-based, cost-effective interventions: how many newborn babies can we save? Published online March 3, 2005. http:// image.thelancet.com/extras/05art1217web.pdf.
- 67 Bang AT, Bang RA, Baitule SB, Reddy MH, Deshmukh MD. Effect of home-based neonatal care and management of sepsis on neonatal mortality: field trial in rural India. *Lancet* 1999; 354: 1955–61.
- 68 Manandhar DS, Osrin D, Shrestha BP, et al. Effect of a participatory intervention with women's groups on birth outcomes in Nepal: cluster-randomised controlled trial. *Lancet* 2004; 364: 970–79.